Claims

1. An method for identifying and/or obtaining a compound which inhibits infectivity of a protozoan pathogen, which method comprises:

(a) contacting an isolated Rhomboid polypeptide and an isolated substrate polypeptide in the presence of a test compound; and

(b) determining proteolytic cleavage of the substrate protein.

2. A method according to claim 1 wherein the protozoan pathogen is an apicomplexan pathogen.

3. A method according to claim 2 wherein the apicomplexan pathogen is selected from the group consisting of Plasmodium, Toxoplasma, Eimeria, Sarcocystis, Cyclospora, Isospora, Cryptosporidium, Babesia and Theileria.

4. A method according to any one of the preceding claims wherein the Rhomboid polypeptide is a protozoan Rhomboid protein

5. A method according to claim 4 wherein the Rhomboid polypeptide is encoded by a nucleic acid sequence shown in Table 1.

6. A method according to any one of the preceding claims wherein the substrate polypeptide comprises a lumenal domain and a TMD, the TMD having a region proximal to the lumenal domain which comprises one or more of residues 138-144 of the Drosophila Spitz sequence (ASIASGA).

7. A method according to claim 6 wherein the substrate polypeptide comprises a TMD and a lumenal domain, the TMD having a region proximal to a lumenal domain which has the sequence of residues 138-144 of Drosophila Spitz.

8. A method according to claim 6 wherein the substrate polypeptide is an adhesive micronemal polypeptide.

9. An assay method according to claim 8 wherein the substrate polypeptide is encoded by a nucleic acid sequence shown in Table 2.

10. An assay method according to claim 9 wherein the substrate polypeptide is Ama-1 or CTRP.

11. A method according to any one of the preceding claims wherein the substrate polypeptide and the Rhomboid polypeptide comprise ER (endoplasmic reticulum) retention signals.

12. A method according to claim 10 wherein the endoplasmic reticulum retention signals are KDEL or KKXX.

13. A method according to any one of the preceding claims wherein the substrate polypeptide comprises an extracellular domain having a detectable label.

14. A method according to claim 13 wherein the detectable label is GFP.

15. A method according to any one of the preceding claims wherein said Rhomboid polypeptide and said substrate

polypeptide are expressed in a host cell from heterogeneous nucleic acid.

16. A method according to any one of the preceding claims comprising the further step of;

(c) bringing into contact an isolated human Rhomboid polypeptide and a polypeptide substrate in the presence of the test compound; and,

(d) determining proteolytic cleavage of the substrate by the human Rhomboid polypeptide.

17. A method according to any one of the preceding claims comprising identifying said test compound as a modulator of adhesive micronemal polypeptide cleavage.

18. A method according to claim 17 further comprising determining the ability of said test compound to inhibit the invasiveness of a protozoan pathogen.

19. A method according to claim 17 or claim 18 comprising isolating said test compound.

20. A method according to claim 19 comprising synthesising the test compound.

21. A method according to claim 19 comprising modifying the test compound to optimise its pharmacological properties.

22. A method according to any one of claims 17 to 21 comprising formulating said test compound in a pharmaceutical composition with a pharmaceutically acceptable excipient, vehicle or carrier.

23. A compound which modulates protozoan pathogen infectivity obtained by a method of any one of claims 1 to 18.

24. A compound according to claim 23 comprising a peptide fragment of a protozoan Rhomboid polypeptide.

25. A method of producing a pharmaceutical composition comprising;

identifying a compound which inhibits the infectivity of a protozoan pathogen using a method according to any one of claims 1 to 18; and,

admixing the compound identified thereby with a pharmaceutically acceptable carrier.

26. A method according to claim 25 comprising the step of modifying the compound to optimise the pharmaceutical properties thereof.

27. A method for preparing a pharmaceutical composition for treating a protozoan pathogen infection comprising;
i) identifying a compound which modulates the proteolytic activity of a Rhomboid polypeptide,
ii) synthesising the identified compound, and;
iii) incorporating the compound into a pharmaceutical composition.

28. A pharmaceutical composition comprising a compound according to claim 23 or claim 24.

29. Use of a compound according to claim 23 or claim 24 in the manufacture of a composition for treatment of a protozoan pathogen infection.

30. A method comprising administration of a composition according to claim 23 or claim 24 to a patient for treatment of a protozoan pathogen infection.

31. A method according to claim 30 wherein the protozoan pathogen is an apicomplexan pathogen selected from the group consisting of Plasmodium, Babesia, Theileria, Toxoplasma, Eimeria, Sarcocystis, Cyclospora, Isospora and Cryptosporidium.

32. A method of identifying a protozoan Rhomboid polypeptide comprising;

(a) providing a test protozoan Rhomboid polypeptide,

(b) bringing into contact a substrate polypeptide and the test Rhomboid polypeptide under conditions in which the substrate polypeptide is normally proteolytically cleaved; and,

(c) determining cleavage of the substrate polypeptide.

33. A method according to claim 32 wherein the test Rhomboid polypeptide comprises an amino acid sequence encoded by a nucleic acid sequence shown in Table 1.

34. A method according to claim 32 or claim 33 wherein the substrate polypeptide comprises the lumenal region of the TMD of Spitz, Gurken, Keren, Ama-1 or CTRP.

35. A method according to any one of claims 32 to 34 wherein the substrate polypeptide comprises an amino acid

sequence encoded by a nucleic acid sequence shown in Table 2.

36. A method according to claim 35 wherein the substrate polypeptide is Ama-1 or CTRP.